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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,077	02/07/2002	Daniel R. Gallie	02307O-121500US	9447

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 06/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/072,077	GALLIE ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/15/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-27 are pending and are examined in the present office action.

Specification

2. The attempt to incorporate subject matter into this application by reference to Gan et al (1995, Science, 270:1986-1988, listed in the IDS) is improper because Applicant relies on the Gan et al reference for essential material, i.e., the sequence of the pSG516 construct which comprises the nucleic acid sequence encoding the isopentenyl transferase (IPT) protein. In fact, the Gan et al reference cites another reference, Li et al (1992, Dev. Biol. 153:386) which supposedly discloses the nucleic acid sequence encoding IPT. Said reference has been placed on form 892 so that said reference will be printed upon issuance of a patent for the present application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to methods and a transgenic maize plant comprising a programmed cell death inducible promoter, a promoter from a floret specific gene associated with cell death, or wherein said promoter is not associated with cell death, a SAG12 promoter or a promoter that is 70% identical to SEQ ID NO:1 operably linked to a nucleotide sequence that inhibits programmed cell death, a nucleotide sequence encoding a plant growth regulator synthesizing enzyme, wherein the enzyme catalyzes the synthesis of cytokinin, or wherein the enzyme is any isopentenyl transferase.

Applicants disclose introducing construct pSG516 comprising a SAG12 promoter operably linked to an IPT gene into maize embryogenic callus and regenerating plants that were crossed with inbred line B73 (page 18, Example 1).

The Applicants do not identify essential regions of any cell death inducible promoter, any promoter from a floret specific gene, any SAG12 promoter or any promoter that is 70% identical to SEQ ID NO:1; nor do Applicants identify any essential regions of any nucleotide sequence that inhibits programmed cell death, any nucleotide sequence encoding a plant growth regulator synthesizing enzyme or any nucleotide sequence encoding any isopentenyl transferase. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may

be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of polynucleotide sequences that are cell death inducible promoters, or promoters that are from floret specific genes that are and are not associated with programmed cell death, or SAG12 promoters, or that are promoters that exhibit 70% identity with SEQ ID NO:1. In addition, Applicants fail to describe any nucleotide sequence that inhibits programmed cell death, or wherein the nucleotide sequence encodes any plant growth regulator synthesizing enzyme, or any isopentenyl transferase. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for any programmed cell death inducible promoter, SAG12 promoter, or an nucleotide sequence that inhibits programmed cell death, or that encodes any plant growth regulator synthesizing enzyme or any isopentenyl transferase (IPT), it remains unclear what features identify any of the claimed sequences. Since the genus of programmed cell death inducible promoters, SAG12 promoters, nucleotide sequences that inhibit programmed cell death or that encode any plant growth regulator synthesizing enzyme or any IPT have not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Scope of Enablement

4. Claims 1-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a construct comprising the nucleic acid sequence encoding the isopentenyl transferase (IPT) protein used by Applicant operably linked to the Arabidopsis senescence-associated SAG12 promoter introduced into embryogenic maize callus, plants regenerated from the embryogenic callus and transgenic plants exhibiting two embryos and fused endosperm in the maize seeds, does not reasonably provide enablement for claims drawn to a method of inhibiting programmed cell death in a maize plant or a transgenic maize plant comprising introducing a construct comprising a programmed cell death inducible promoter operably linked to a nucleotide sequence that inhibits programmed cell death, wherein the nucleotide sequence encodes a plant growth regulator synthesizing enzyme, wherein the enzyme catalyzes the synthesis of cytokinin, or wherein the programmed cell death inducible promoter is any SAG12 promoter or any SAG12 promoter exhibiting 70% identity to SEQ ID NO:1 or wherein the promoter is from a floret specific gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior

art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to methods of inhibiting programmed cell death in a maize plant and a transgenic maize plant comprising a programmed cell death inducible promoter, a promoter from a floret specific gene associated with cell death, or wherein said promoter is not associated with cell death, a SAG12 promoter or a promoter that is 70% identical to SEQ ID NO:1 operably linked to a nucleotide sequence that inhibits programmed cell death, a nucleotide sequence encoding a plant growth regulator synthesizing enzyme, wherein the enzyme catalyzes the synthesis of cytokinin, or wherein the enzyme is any isopentenyl transferase.

Applicants disclose introducing construct pSG516 comprising a SAG12 promoter from Arabidopsis operably linked to an IPT gene into maize embryogenic callus and regenerating plants that were subsequently crossed with inbred line B73. Progeny from the cross were hemizygous for the SAG12::IPT construct and were self pollinated and the resulting kernels exhibited two embryos with a fused endosperm and segregated with the segregating population (page 18, Example 1).

Applicants have not disclosed which nucleic acid sequence encoding IPT was used in Example 1. Applicants have not disclosed any nucleotide sequence that inhibits any programmed cell death, or encodes any plant growth regulator synthesizing enzyme, or wherein the enzyme catalyzes the synthesis of cytokinin. Applicants have also not disclosed any programmed cell death inducible promoter from any plant, or any promoter from any floret specific gene that is and is not associated with cell death or any promoter that is 70% identical to SEQ ID NO:1.

Applicants have not disclosed how one identifies or isolates any programmed cell death inducible promoter from any plant, or any promoter from any floret specific gene that is and is not associated with cell death or any promoter that is 70% identical to SEQ ID NO:1. In addition, Applicants have not disclosed how one identifies or isolates any nucleotide sequence that inhibits any programmed cell death, or encodes any plant growth regulator synthesizing enzyme, or wherein the enzyme catalyzes the synthesis of cytokinin. Applicants have not taught which regions of the respective polynucleotides can be used to amplify any of said polynucleotides or which regions can be used as a probe to isolate any of said polynucleotide sequences.

The state-of-the-art teach that transforming a plant with a cell death suppressing gene produces unexpected results. Mittler et al (1996, The Plant Cell 8:1991-2001) teach tobacco plants transformed with a cell death suppressing gene showed no decrease in cell death when plants were infected with tobacco mosaic virus or *Psuedomonas syringae*, both of which induce programmed cell death in plants (page 1996, right column, 2nd paragraph).

Using pieces of a promoter that do not contain the full compliment of cis-acting elements, will not produce the expression profile as observed using the whole promoter fragment. Benfey et al (1990, Science 250:959-966) teach that the 35S CaMV promoter consists of domains that individually regulate spatial expression within plants. "The combination of each of the five B subdomains with domain A results in an expression pattern that differs from that of the individual subdomains or domain A" (page 961, left column, 2nd paragraph). In other words, deleting a required domain will jeopardize the proper spatial and temporal expression pattern. In addition, Benfey et al (1989, EMBO J, 8(8):2195-2202; page 2200, left column 2nd paragraph)

teach that not only are the promoter domains important for specifying proper spatial and temporal expression but that when all domains were present, the quantity of expression increased.

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through all the promoter sequences of a plant to find those that are programmed cell death inducible, and to screen through all the nucleic acid sequences encoding proteins to find any that inhibit programmed cell death, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed in a plant inhibit programmed cell death in the lower floret of maize plants.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amasino et al (November, 1997, U.S. Patent Number 5,689,042, listed in IDS).

The claims are drawn to methods of inhibiting programmed cell death in a maize plant and a transgenic maize plant whereby programmed cell death in the lower floret is inhibited comprising a programmed cell death inducible promoter, a promoter from a floret specific gene associated with cell death, or wherein said promoter is not associated with cell death, a SAG12 promoter from Arabidopsis or a promoter that is 70% identical to SEQ ID NO:1 operably linked to a nucleotide sequence that inhibits programmed cell death, a nucleotide sequence encoding a plant growth regulator synthesizing enzyme, wherein the enzyme catalyzes the synthesis of cytokinin, or wherein the enzyme is any isopentenyl transferase.

Amasino et al teach a genetic construct comprising an Arabidopsis-derived SAG12 promoter operably linked to a DNA sequence encoding an isopentenyl transferase and a transgenic plant transformed with said construct wherein the foreign genetic construct is expressed in tissues entering senescence to delay the senescence of the plant tissues (columns 19-20, claims 1, 8-9, 14-17 and 20).

Amasino et al do not teach transformation of maize.

Given the recognition of those of ordinary skill in the art of the value of producing plants with altered senescence characteristics by transforming a plant with the genetic construct of Amasino et al as disclosed above, and as disclosed by Amasino et al (column 6, lines 18-41), it would have been obvious to introduce said construct into a maize plant for the purpose of altering the senescence of the lower floret, thereby producing more flowers as taught by Amasino et al (*ibid*) which would result in two embryos per seed, absent evidence to the contrary or absent evidence of unpredictability of transforming a maize plant with said construct. It is noted that in maize, there are two florets per spikelet and the upper floret develops into the corn

kernel (seed) and only the lower floret goes through programmed cell death. Therefore, the only floret that can have programmed cell death inhibited is the lower floret.

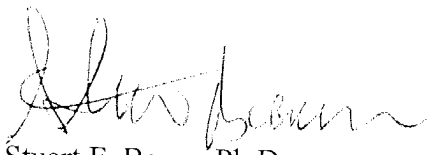
Thus the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

6. No claims are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
June 10, 2004